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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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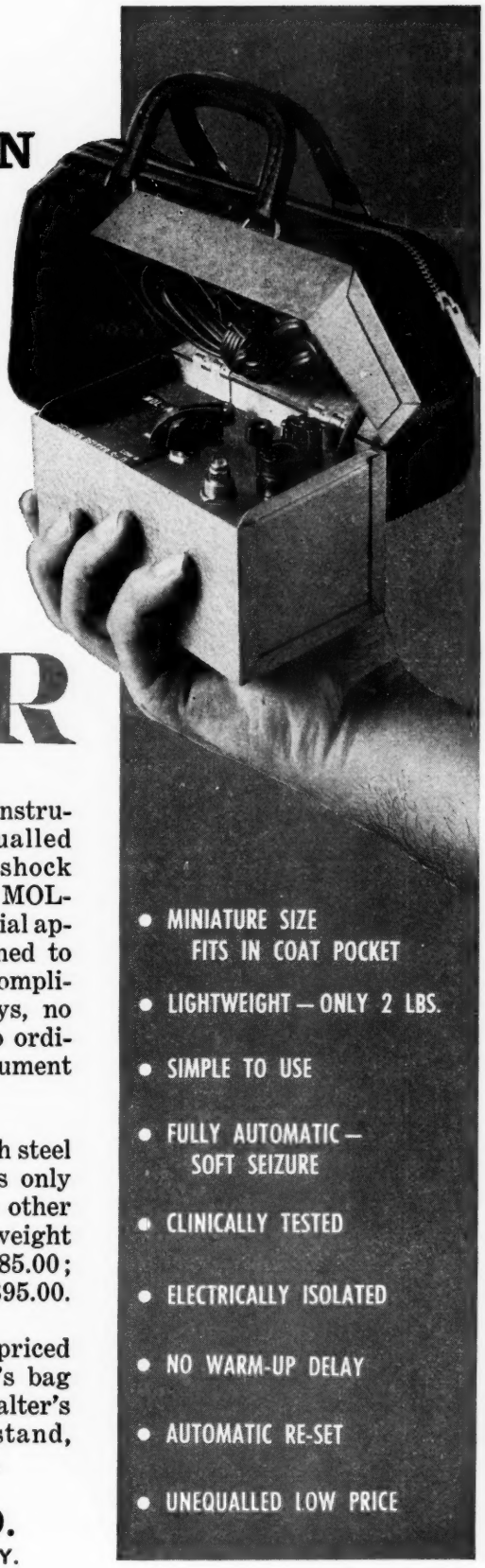

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DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

The Funkenstein Test in Selecting Methods of Psychiatric Treatment

CHARLES H. JONES, M.D.
Sedro Woolley, Washington

In the fall of 1953 two newly purchased books arrived at Northern State Hospital. The first was "Treatment of Mental Disorders" by Leo Alexander;[1] the other was "Physiological Foundations of Neurology and Psychiatry" by Ernst Gellhorn.[2] As these books were perused it was seen that together they presented a strikingly logical case for the routine use of the Funkenstein test before starting any physiological type of psychiatric treatment. The arguments for the use of the test as developed in these texts so complemented each other that it was concluded that the test was probably in routine use in most mental hospitals. Therefore, in trying the test at Northern State Hospital, it was believed that we were catching up with other institutions in taking advantage of this advance in psychiatry which allows a more specific selection of patients for treatment. A few dozen tests were tried and were seen to have such practical value that a routine screening program was established in February 1954 on the female receiving and treatment wards. By the fall of 1954 a similar routine screening program was in operation on the male service. To date 747 Funkenstein tests on 465 patients have been completed and it appears that instead of catching up with other mental hospitals we are perhaps somewhat in the lead in using this test on a routine basis.

In 1948 Funkenstein, Greenblatt and Solomon[3] reported the use of a test of the autonomic nervous system on 50 hospitalized mentally ill patients before and after convulsive shock therapy. In their series the test was performed within three days of the initial electric shock and was repeated within two to five days after completion of the courses of treatment. The test consisted of three procedures, one on each of three successive days. In each instance the patient's blood pressure and pulse were taken until constant for a five minute period following bed rest. The first day, patients received 1 cc. of normal saline intravenously; the second day .05 mgms of adrenalin chloride in .5 cc. of water were injected intravenously; on the third day mgms of mecholyl were given intramuscularly. During the first two procedures the systolic blood pressure was recorded rapidly until it had returned to the previous resting level. On the third day the systolic blood pressure was recorded every four minutes for 25 minutes after the injection of mecholyl. Objective autonomic phenomena such as sweating, tremor, flushing or pallor were noted. When the examinations were completed the patients were asked about anxiety and, if produced, whether such was similar to that which might have been experienced during clinical attacks. Also the patients were asked whether or not mecholyl

From Northern State Hospital, Sedro Woolley, Washington.
Read March 1, 1955 to the Oregon Neuropsychiatric Society, Portland, Oregon.

relieved anxiety. Graphs were made from the blood pressure recordings, using the systolic blood pressure as the ordinate and the time as the abscissa. From the findings on the fifty patients it was possible to delineate seven different patterns of response to the two drugs, adrenalin and mecholyl.

Although the authors did not report on the amount of electric shock which was given to any of the group, two classifications were made following treatment. "Improved" meant that patients had maintained improvement sufficient to allow discharge from the hospital within ten days to two weeks after termination of treatment; "unimproved" meant that patients failed to show sufficient improvement with electric shock to enable them to leave the hospital or that they were unable to leave without another type of treatment.

From an analysis of clinical results as related to seven different reactive groups it was very clearly demonstrated that patients in hyporeactive groups 6 and 7 were markedly responsive to convulsive electroshock, whereas, those in the other groups were relatively unresponsive. It was seen that there was no specific diagnostic distribution in the various groups, although patients suffering from involutional psychoses and manic depressive psychoses were clustered in groups 6 and 7. In comparing the post-treatment responses to the injected drugs it was noted that electroshock tended to cause a shift from the higher numbered groups to the lower. Funkenstein, Greenblatt and Solomon concluded that a good prognosis with convulsive electroshock therapy could be predicted if the patient showed an initial autonomic grouping in 6 or 7, if anxiety was precipitated or relaxed by mecholyl or if a chill was experienced after mecholyl.

In 1949 the same authors[4] reported on 115 cases either hospitalized or attached to their outpatient clinic. They reported that there was a reciprocal relationship between the immediate increase in blood pressure from adrenalin and the immediate fall with mecholyl, the greater the increase from adrenalin the less fall with mecholyl. Not only was a greater rise in blood pressure with adrenalin associated with a smaller drop with mecholyl but also the degree of delayed rise above the resting level was correspondingly greater. The responses of the 115 patients were compared with a group of controls. The controls showed moderate responses and early re-establishment of homeostasis. The patient's responses were either exaggerated or weak and were often associated with a deficient capacity to re-establish homeostasis. In another study[5] of 24 patients who were followed closely after treatment, these workers concluded that a return of a patient's response toward his initial reaction prior to treatment, indicated that a relapse would occur if such were not already apparent.

In 1951 Funkenstein and his colleagues[6] reported on the relationship of autonomic to psychologic changes in various types of mental illness. They observed that clinical improvement was associated with changes in patients' responses to adrenalin and mecholyl toward moderate reactions and prompt homeostasis regardless of what type of treatment was used—electroshock, insulin or psychotherapy. The same phenomenon was observed in patients who recovered spontaneously. Also, with normal controls they noted that stress was associated with an autonomic imbalance with these drugs, which imbalance was not demonstrable when stress was absent. In the same report the flat statement was made that they never had had a case in which anxiety was precipitated by adrenalin in which electroshock had not made the patient clinically more anxious. They also observed that patients who were clinically improved after insulin coma therapy no longer demonstrated adrenalin precipitable anxiety, whereas, such was often a feature of the test before treatment.

Gellhorn[2] devotes an entire chapter of his book to an evaluation of the Funkenstein test in light of experimental work on animals in his laboratory. He develops the concept that central autonomic dysfunction probably underlies psychic disorders and that a determination of the nature and extent of such dysfunction offers clues as to what form of treatment might be beneficial. According to Gellhorn "the most important finding of Funkenstein et al., is the fact that when the psychological picture changes the physiological picture changes and vice versa;

that is, improvement or impairment of the clinical condition of the patient is associated with an alteration in the blood pressure reactions that are induced by mecholyl and adrenalin. If these reactions do not change the clinical picture is unaltered. Moreover, certain changes in these autonomic reactions are associated with clinical improvement regardless of the means by which the clinical (psychological) changes of the patient's condition are brought about." Gellhorn demonstrated the relation of the posterior hypothalamus and reactivity of the sympathetico-adrenal system to mecholyl with several animal experiments. Small doses of mecholyl produced a depressed blood pressure response in normal animals from which a rapid recovery was made. In cats having bilateral coagulated lesions of the posterior hypothalamus, however, the hypotensive reaction to mecholyl seemed to be prolonged and greatly aggravated. The same phenomenon was noted in animals with hypothalamic injections of pentothal or procaine. With stimulation of the hypothalamus with near threshold electrical currents and with hypothalamic injections of minute quantities of strychnine the hypotensive action of mecholyl was followed by a blood pressure rise well above the resting level.

Unpublished work with Sigg and Koella is mentioned by Gellhorn to show that the hypotensive action of mecholyl is responsible for the activation of the hypothalamus. These workers used diencephalic and cortical electrodes to indicate that as the blood pressure returns to normal after the injection of mecholyl, excitation of the hypothalamus and thalamus are simultaneously associated with a generalized cortical excitation.

From these experiments Gellhorn concludes that "the degree and particularly the duration of the hypotensive action of mecholyl and the reflexly induced discharges of the sympathetico-adrenal system depend on the hypothalamus" and that "apparently conditions leading to increased sympathetic discharges of the hypothalamus as the result of electrical or chemical stimulation augment the responsiveness of the sympathetico-adrenal system to mecholyl and lead to a quicker return of the blood pressure and/or an overcompensatory hypertensive phase." Thus for practical purposes it appears that the simple mecholyl test gives a satisfactory indication of central sympathetic reactivity if one concludes that the homeostatic recovery of blood pressure from mecholyl induced hypotension depends upon hypothalamic sympathetic discharges.

In light of considerations mentioned thus far it seems logical to consider that the efficacy of convulsive electroshock is related to a shift in hypothalamic sympathetic excitability from hyporeactivity toward hyperreactivity, that convulsive electroshock therapy is specifically indicated in patients demonstrating hyporeactive sympathetic centers and is specifically contraindicated in patients with hyperreactive sympathetic centers. Likewise, nonconvulsive electroshock which is capable of producing shifts from central sympathetic hyperreactivity to hyporeactivity should be prescribed only for those patients with hyperreactive responses to the Funkenstein procedure.

Alexander[7] particularly stresses the fact that nonconvulsive shock acts in a manner opposite to convulsive electric shock. He reports excellent results with the nonconvulsive method when convulsive electric shock has produced confusion and disorientation to a degree contraindicating further treatment. With this combination he is able to continue and extend courses of treatment. Alexander elaborates in his new book that nonconvulsive electric shock therapy causes effects opposite to those of convulsive electric shock. It reduces adrenalin precipitable anxiety, enhances and prolongs the fall of blood pressure after the injection of mecholyl, lowers the psychological defencses and may provoke depression. In other words, nonconvulsive electroshock changes Funkenstein responses from the lower to the higher classifications, just the opposite of convulsive electroshock.

Until the arrival of the books by Gellhorn and Alexander the staff at Northern State Hospital had been using convulsive electroshock extensively on an empirical basis. Results were largely dependent upon the experience of individual staff members, many of whom were newcomers to psychiatric practice. In addition to several instruments

designed for convulsive electroshock therapy one Reiter model CW-46 machine was in use. Nonconvulsive electroshock was given with this machine on a few patients empirically but for the most part it was used to treat patients who constituted high risks for convulsive electroshock and to clear up states of confusion and/or excitement produced by convulsive electroshock. Likewise at that time patients were selected empirically for insulin coma therapy. This form of treatment was usually reserved for young patients who had not completely improved or who had not maintained improvement brought about by convulsive electric shock. As previously outlined, Gellhorn and Alexander firmly state that convulsive electroshock therapy offers good results only for those patients showing central sympathetic hyporeactivity and is specifically contraindicated for those showing central sympathetic hyperreactivity; also that the opposite is the case for nonconvulsive electroshock therapy and that schizophrenic patients showing neither response are best treated by insulin coma therapy. These authors were so forthright in their statements that it appeared to us it would be unscientific to prescribe any form of physiological treatment without first doing a Funkenstein examination. We concluded, therefore, that the test would be of practical administrative value in an institution such as ours to help screen patients for physiological treatment.

Certain modification of the procedure appeared in order, however, if it were to be put to routine use. We did not intend to conduct a program of clinical investigation or to check on the validity of the test. All that was desired was information which would help in the selection of physiological treatment for individual patients. Therefore, to begin with, the seven Funkenstein classifications were discarded. Next, the various procedures were adjusted to that the test could be accomplished in one day. The saline injection was eliminated entirely. Patients were put to bed for one hour before the test, and blood pressure was recorded every five minutes during the second half hour. It was decided to do the mecholyl part of the test first as often central sympathetic hyporeactivity or hyperreactivity can be demonstrated by this drug alone. This part of the test has been carried out as described by Funkenstein with the injection of 10 mgm. of mecholyl into the buttocks and the charting of systolic blood pressure at four minute intervals along with any striking objective autonomic responses. No attempt has been made to interview patients after the test. With a hyporeactive response to mecholyl evidence is obtained which suggests convulsive electroshock and consequently there is no need to give adrenalin. Likewise, if there is marked elevation of systolic blood pressure above the resting level, there is evidence that the patient is showing central sympathetic hyperreactivity. Thus it is seen that convulsive electric shock is contraindicated and that some form of treatment such as nonconvulsive electroshock should be considered. In case patients show a prompt return of systolic blood pressure to the resting level with little or no overriding, adrenalin is injected. This is done at the end of the twenty-four minutes after mecholyl as the graphs customarily show twelve to sixteen minutes of stabilized blood pressure in this type of response. As suggested by Alexander the dose of adrenalin has been cut in half from that originally recommended by Funkenstein and it has been found that .025 mgm works quite well.

At the start of the program five patients were tested each week, as mecholyl comes in 25 mgm ampules and two ampules thus provide 10 mgms for five patients. Although the medical staff was slow to order Funkenstein tests at first, in a very short time requests for them became so great that on some weeks as many as 15 tests were done. As the program expanded it was noted that the modifications which allowed the test to be performed in a single day did not interfere with the utility of the information obtained. With very rare exceptions systolic blood pressure was easily stabilized at a resting level and was not psychologically modified by the activities of the personnel carrying out the test. In 747 trials minor complications occurred six times. Five asthmatic attacks were precipitated but were readily controlled by intravenous atropine. One patient complained of severe substernal pain which slowly subsided after atropine. Two

known asthmatics and one known cardiac patient were given 5 mgms. of mecholyl instead of 10 and satisfactory graphs were obtained without complications.

Most findings of Funkenstein et al., and Alexander can be confirmed on the basis of clinical experience with the 747 trials with 465 patients. Central sympathetic hyporeactivity was invariably seen in retarded manic depressive patients and those with involutional melancholia. Patients with agitated depression customarily demonstrated central sympathetic hyperreactivity. Schizophrenic patients showed both hyporeactive and hyperreactive responses as well as no demonstrable central sympathetic dysfunction. Although diagnostic formulations were made by a dozen different doctors and were not subject to careful scrutiny, it developed that most disturbed patients having the diagnosis of catatonic schizophrenia showed central sympathetic hyporeactivity, whereas, paranoid, pseudoneurotic and retarded catatonic schizophrenics tended to show central sympathetic hyperreactivity or no disturbance in central autonomic homeostasis.

The efficacy of convulsive electroshock therapy was conclusively demonstrated for those patients showing central sympathetic hyporeactivity. The only patients of this group who did not get well were those suspected of having organic illnesses or who demonstrated tenacious paranoid trends. Early in the program tests were given to patients who had previously received convulsive electroshock with poor results, often with the precipitation of states of excitement. When these patients were tested after periods of convalescence most showed central sympathetic hyperreactivity. Also early in the program a few patients with no demonstrable imbalance of the central homeostatic mechanism were given convulsive electroshock empirically but none were substantially improved as the result of treatment. Clinically we found nonconvulsive electroshock very beneficial for patients showing central sympathetic hyperreactivity.

One observation of Funkenstein, Greenblatt and Solomon and of Alexander cannot be confirmed at this time. This is the finding that physiological changes parallel psychological changes. They noted that as patients improved the Funkenstein response changed to normal and if relapses occurred the original Funkenstein response returned. The reason this observation cannot be confirmed is that the program was not set up to check this point. A return to normal or towards normal was noted in many improved patients. However, others improved with autonomic abnormalities persisting in post-treatment tests. As many of these patients maintained their improvements, there was no further occasion to perform tests to see whether or not additional treatment was necessary. If such patients did not maintain their improvements, however, information from post-treatment Funkenstein examinations was often used to determine what type of additional treatment would be given. Therefore, for those patients who improved psychologically but still showed central autonomic dysfunction at the end of treatment, it cannot be determined whether or not the Funkenstein response ultimately changed toward normal homeostatic control as the proper times for doing the tests have long since passed.

On the basis of experience with this large group, it appears that doing routine Funkenstein tests prior to prescribing physiological treatment results in a more specific selection of the kind of treatment. Convulsive electroshock therapy is now used for a smaller percentage of patients here than was the case before the routine screening program was inaugurated. On the other hand longer courses of treatment are being given and additional courses are being prescribed more frequently. Thus patients for whom convulsive electroshock appears to be specifically indicated have not been abandoned after inadequate trials of treatment.

The practical value of the Funkenstein test has been especially well demonstrated when used for patients who have received treatment privately prior to admission. Before starting this program it was often necessary to wait a month or six weeks before clinical indications for additional treatment could be determined. Prior treatment had often obscured the symptomatology of the illnesses, yet had not been given in amounts sufficient

to sustain remissions. With the use of the Funkenstein examination supplementary treatment could be started without delay. Occasionally treatment opposite in effect to that which had been previously given elsewhere was ordered.

A most striking extra dividend of the Funkenstein routine is the fact that the medical and nursing staffs have come to rely upon the concept of central sympathetic dysfunction and its relation to mental disorders in their clinical thinking and in teaching programs. Recent claims for certain drugs which have been given to mentally ill patients on an empirical basis have been evaluated in light of this concept. Apparently in most reported series patients have been empirically selected for treatment with Thorazine and Serpasil on the basis of diagnostic categories.[8,9] Theoretically we have speculated that both drugs would be helpful for patients with central sympathetic hyperreactivity and contraindicated for those with central sympathetic hyporeactivity. This anticipation is in harmony with a report[10] on the production of five severe depressions in patients receiving Serpasil for hypertension, some of which depressions required convulsive electroshock. As a preliminary to setting up a program to investigate this hypothesis, Funkenstein tests were performed on six patients prior to receiving Serpasil. Two showed prompt homeostasis; two were hyperreactive; two were hyporeactive. Three days after starting the drug, the intramuscular injection of 5 mgms of mecholyl (half the usual test dose) produced a marked shift toward hyporeactivity in all six patients.

During the past year preliminary evaluations have been made here of the therapeutic effectiveness of the drug, Betasyamine, and of peripheral electrical stimulation as related to Funkenstein test changes.[11] It appears that both forms of treatment are of value for patients showing central sympathetic hyperreactivity but do not benefit those showing central sympathetic hyporeactivity. Recently with the Funkenstein screening routine definitely established and working smoothly, an investigative program has been started which is essentially as follows: All patients whose clinical status indicates the need of physiological treatment and whose Funkenstein responses show hyperreactivity of ten points or more above the resting systolic blood pressure level, are screened for a project which compares four forms of treatment, Betasyamine, peripheral electrical stimulation, Thorazine and Serpasil, each of which is thought to be of merit for patients with central sympathetic hyperreactivity. A project roster has been established with scrambled numbers so that at the time a patient is placed on the project the exact type of treatment will be unknown to the physician until the person with the key has been consulted. It is contemplated that the drugs will be administered for a period of two months and that 20 peripheral electrical stimulations will be given. In this investigation the Funkenstein test will be repeated at the end of treatment and at weekly intervals for one month after treatment. It is anticipated that with this scheme it may be possible to corroborate the finding that changes in the Funkenstein response parallel psychological changes.

It may be concluded that after sixteen months' experience with Funkenstein tests in 747 trials, we are very satisfied with it as a practical test which yields useful information about individual patients. It has been found to be most helpful in prescribing physiological treatments in a scientific manner. Finally, we are inclined to agree with the opinion advanced by Gellhorn that further investigations into the relation of mental illness to the controls of central autonomic reactivity will yield much information of diagnostic and therapeutic significance.

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Definitive Diagnosis in Loss of Consciousness

(Further Experience With Metrazol Activation)

HENRY A. BRANDT, M.D., and ROBERT P. JEUB, M.D.
Minneapolis, Minnesota

I. *Introduction*

The occurrence of an unexplained disturbance of consciousness in Air Force personnel makes mandatory an exhaustive medical evaluation until a definitive diagnosis is clinically verified. This is justified when we consider the paramount need to insure flying safety. The verification of a convulsive disorder requires permanent grounding in flying personnel and separation from the Air Force for basic trainees. The specialist is required to evaluate these patients for long periods of time until definitive diagnosis can be rendered with certainty.

II. *Problem*

Evaluation of patients who have had an episode of alteration of consciousness is a constant challenge to the specialist and general practitioner alike. The patient giving a history of tonus, clonus, tongue biting, sphincter disturbances, muscle soreness, or amnesia can be readily recognized as a convulsive disorder.

Others presenting momentary disturbances of consciousness with abnormal electroencephalograms likewise produce no difficulty in diagnosis. However, many patients are referred to us because of loss of consciousness without clear-cut histories which would indicate a psychic or organic origin.

The historical data usually discloses a diagnosis of a convulsive disorder in the majority of patients. However, certain patients referred to us give an unreliable history even after repeated consultations, due to illiteracy, emotional blocking or malingering. As a result, other methods to make a diagnosis or delineate abnormalities were desired. A review of the literature on Metrazol was found to be rather inconclusive. A method which would result in a worthwhile correlation of clinical material with Metrazol activated electroencephalograms was considered practical. In the study of 100 patients, 56 had previous neuropsychiatric workups without disclosure of psychic or organic abnormalities and 92 had normal routine electroencephalograms with hyperventilation.

III. *Review of Literature*

A—CONTROL STUDIES

Many objections may be raised concerning the reported Metrazol activation in control groups of patients. Of prime importance is the realization that any individual will respond with a clinical seizure if given adequate dosage of Metrazol rapidly enough. The selection of a control group free of psychiatric disorders, especially those of aggressive character and underlying organic neurological disorders is considered optimum regardless of whether the individual has a past history of loss of consciousness.

Cure[1] using a rapid method (total dose of 2.6 mg per kg initially) reported no activation in six patients. Using a slow tech-

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nique of 20 mg every 30 seconds up to a total of 400 mg, activation was found in 15% of 31 non-epileptic patients.

Merlis[2] using a technique of 25 mg every 30 seconds up to 500 mg, observed no activation in 38 subjects.

Peniche[3] using 200 mg of Metrazol in a 10% solution intravenously in 1 minute, found 6% activation in 100 psychiatric patients.

Cohn[4] using 100 mg per minute, found activation in 67% of 15 narcoleptic and aggressive patients, and 14% of 118 neuropsychiatric patients.

Fuglsang-Frederikson[5] using 2 mg/kg of body weight initially, followed by 1 mg/kg at 30 second intervals up to 350 mg., found 1.6% activation in 63 subjects.

Smith[6] using a rapid intravenous dose with increasing dosage at subsequent tests, found paroxysmal activation in 33% of 48 non-epileptic neuropsychiatric patients.

Browne-Mayers and Straub[7] using a technique of 20 mg every 30 seconds up to 400 mgs found paroxysmal activation in 20% of 61 non-epileptic psychiatric patients with all activation occurring in those with abnormal or "epileptoid" indications in their routine electroencephalograms.

Buchtal and Lennox[8] using 2 mg per kg of body weight intravenously initially, followed by 1 mg per kg of body weight every 30 seconds up to 300 mg found in 682 Air Force applicants activation in 15% of those with normal routine electroencephalograms.

TABLE I

CONTROLS USING METRAZOL

Author	Number of patients	Activation	Method mgm/sec IV	Maximum Dosage
Cohn et al.	15	67%	100/60	300
Cure et al.	31	15%	20/30	400
Merlis et al.	38	0	25/30	500
Smith et al.	48	33%	Rapid IV	300
Moore et al.	59	54%	50/60	500
Brown-Mayers & Straub	61	20%	20/30	400
Fuglsang-Frederiksen	63	1.6%	70/30	490*
Peniche	100	6%	100/30	200
Buchtal and Lennox	682	15%	70/30	440*

*Rapid initial dose of 2 mgms/kg (140 mgms).

Moore, Kellaway and Kagawa[9] using 50 mg every minute up to 500 mg in 120 patients found activation in 54% of those under the age of 30 years (59 patients) and 16.4% of those over the age of 30 years (61 patients).

B—ACTIVATION IN EPILEPTICS

Cure et al.[1] using a rapid technique of (2.6 mg/kg initial dose) found 48% activation in 55, and 80% activation in 50 epileptics using a slow intravenous injection of 20 mg every 30 seconds to a total dosage of 400 mgs.

Merlis et al.[2] found 47% activation in 57 epileptics using 25 mg every 30 seconds up to 500 mg.

Cohn et al.[4] found activation in 54% of 26 epileptics using 100 mg per minute up to 330 mg.

Fuglsang-Frederikson[5] found 82% activation in 96 epileptics using 2 mg/kg of body weight initially, followed by 1 mg/kg at 30 second intervals up to 350 mg.

Moore et al.[9] found activation in 78% of 49 convulsive disorders using 25 mg every 30 seconds up to 500 mg.

Kaufman and co-workers[10] reported focal activation in 60% of 97 post-traumatic epileptics using 200 mg rapidly intravenously.

Hutchinson[11] activated 83% of 36 epileptics using a rapid technique of (2.6 mg/kg initial dosage) followed by 20 mg every 30 seconds to a total dosage of 400 mg.

Rossen[12] studies 415 similar patients without Metrazol and found 53% had abnormal EEG's; of these, he classified 20% as minimal abnormalities, that is, S-1 and F-1 tracings according to Gibb's classification.[13]

The varied techniques and results and lack of a study on a large group using a standardized routine, leaves the value of Metrazol activation in doubt. At present, only a comparison of activation results with clinical findings can confirm the usefulness of the technique.

An attempt was made by us in the following analysis to evaluate certain clinical and fundamental data, which might aid in the differential diagnosis between a so-called idiopathic convulsive episode and unexplained syncopal attacks, as seen in a heterogenous group of patients including the va-

rious psychoneurotic and personality disorders. To accomplish this, careful EEG studies with Metrazol were combined with intensive clinical studies. Organic physiological abnormalities (metabolic, cardiac, stress, etc.) were excluded.

IV. *Metrazol Procedure*

The tracings were performed using solder electrodes and Bentonite paste. Electrodes were placed following the method of Jasper. With the patient reclining, a routine study was performed, including hyperventilation for three minutes and three minutes post-hyperventilation. A solution of Metrazol in normal saline was used (25 milligrams per 1 cubic cm.). The patient was given 100 milligrams per minute intravenously with 1 minute rest between each 100 milligrams. This procedure was carried out until the first paroxysm of spike and slow wave was seen, and in some cases to convulsive thresholds when seizure or abnormal cerebral discharge was observed. Five hundred milligrams was considered maximum. If the patient did not show seizure pattern, hyperventilation was repeated after 500 milligrams and compared with the previous hyperventilation.

V. *Methods of Interpretation*

The interpretation of the routine electroencephalogram was reported as follows: All paroxysmal tracings; spikes; slow activity of 5-7 per second or less; persistent moderate voltage fast activity; and all focal discharges were classified as abnormal. Hyperventilation "build-up" was graded from zero to three plus with no significance attached unless of the "spike and dome" type.

Metrazol activation was considered to be positive when any of the following were elicited: A spike and wave or multiple spike and wave patterns; paroxysmal high voltage slow waves; spikes appearing rhythmically; and focal spike or slow wave abnormalities. The appearance of random, diffuse, moderately fast activity and moderate voltage slow activity was termed "no response" to Metrazol.

The positive Metrazol activations (55 patients) were classified in regard to the initial response (See Table II).

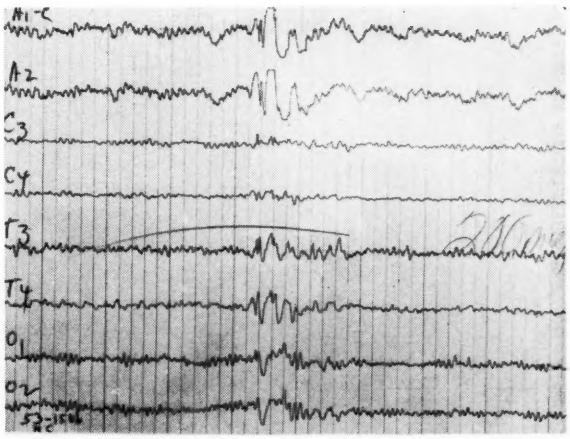


Fig. 1. Showing single spike and slow wave activity with 200 mgms Metrazol.

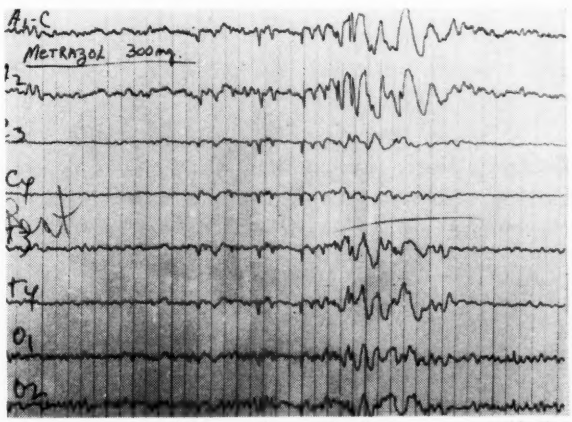


Fig. 2. Multiple spike and slow wave activity, with rest after 300 mgms Metrazol.

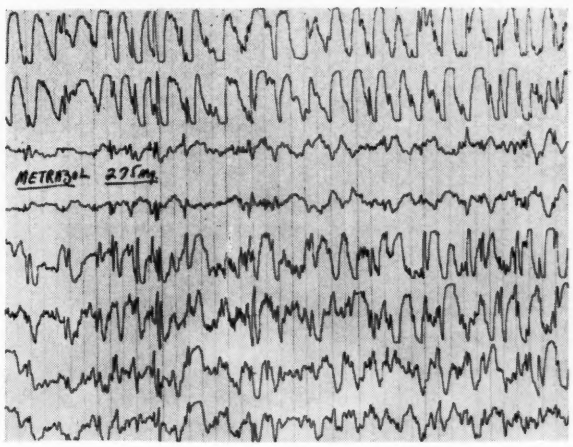


Fig. 3. Continued activity after 275 mgms Metrazol.

The paroxysmal, synchronous, diffuse appearance of the single spike and wave pattern appeared at lower Metrazol dosages and remained distinctly out of context with the recording. At increasing dosages of Metrazol, the paroxysmal, diffuse, multiple spike

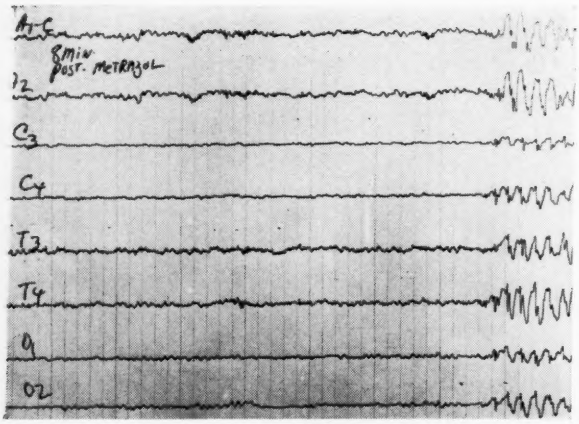


Fig. 4. Multiple spikes and slow waves, post-Metrazol, not hyperventilation.

and wave pattern was more likely to appear and always preceded a grand mal seizure. If continuous activity ensued it was more likely to be of a paroxysmal multiple spike and wave pattern. We believe that the differentiation of these two patterns is essential and the paroxysmal, synchronous, diffuse single spike and wave pattern to be the more infallible criteria.

VI. *Results:*

In records pursued past the initial positive response, there was a mixture of wave patterns. In these cases, the single spike and wave pattern always appeared first. There seems to be justification for assigning more significance to the single spike and wave pattern.

TABLE II

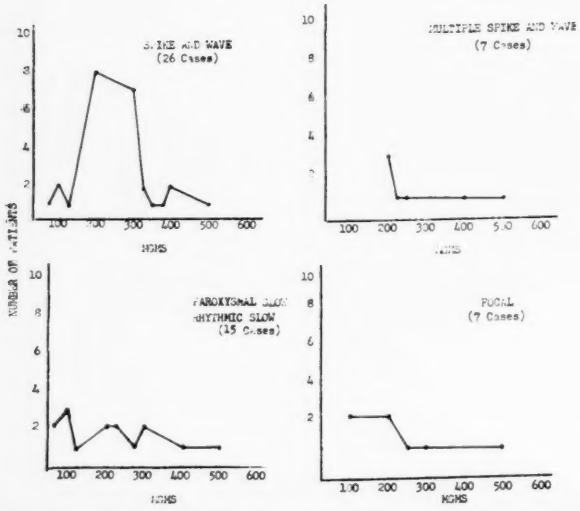
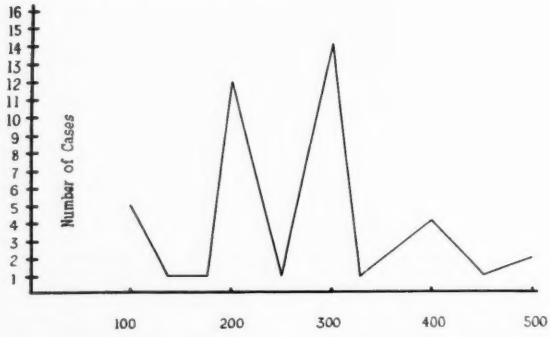


TABLE III

METRAZOL ACTIVATION



The routine electroencephalogram was normal in 92% of this study group. The remaining 8% had mildly abnormal electroencephalograms by our stated criteria. One patient with a left temporal focus on the routine electroencephalogram proved later to have a left sphenoid ridge meningioma.

The median age was 23.62 years, the mean age was 22 years. The oldest was 45 years old and the youngest was 17 years of age.

In 100 patients 55% had a positive response to Metrazol by our criteria. They were broken down as follows:

Organic patients, those giving a history of acute, diffuse, non-progressive disorders, in whom a diagnosis was later established of a toxic, traumatic or infectious process, twelve (12) of nineteen (19) patients, (62%) had a positive response to Metrazol.

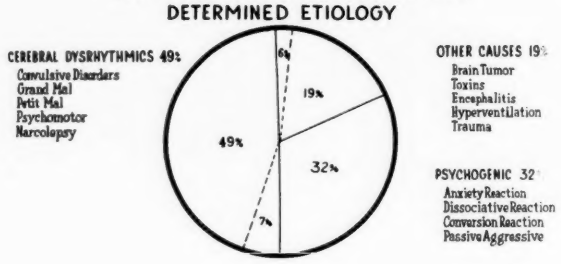
Psychogenic patients, those with syncope (32 patients), all proved later to have posi-

TABLE IV

STUDIES IN SYNCOPE

100 CASES OF UNCONSCIOUSNESS

DETERMINED ETIOLOGY



Thirteen (13) Patients, Seven Convulsive Disorders and Six Organic Disorders Showed 'No Response' to Metrazol.

tive longitudinal histories, psychometrics and interviews. None had a positive response to Metrazol.

In those who were later clinically confirmed as convulsive disorders, 43 of 49 patients (92%), had a positive response to Metrazol.

VII. *Summary:*

One hundred patients with unexplained episodes of loss of consciousness were hospitalized or observed for prolonged periods of time and studies performed until a definitive clinical diagnosis was verified. Physiological abnormalities metabolic, cardiac, stress, etc., were excluded. The objective response to a standardized slow intravenous injection of Metrazol was then correlated. A positive response to Metrazol was found in 92% of 49 convulsive disorders, 62% of 19 organic neurological disorders and 0% of 32 psychogenic disorders. A more significant index of Metrazol activation is given to the paroxysmal, synchronous, single spike and wave pattern. An extremely accurate correlation has been affirmed between the response to Metrazol in the EEG and the verified clinical diagnosis.

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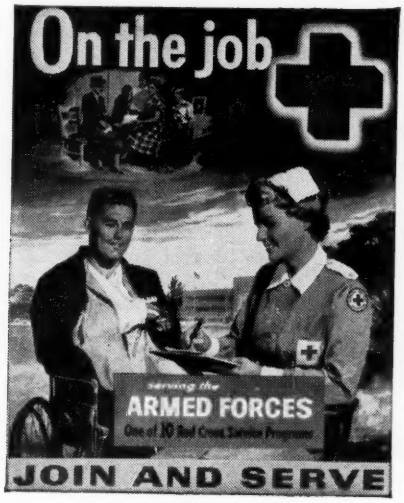

Chlorpromazine in the Treatment of Symptomatically Refractory Conditions in General Paretics

(A Preliminary Report of Seven Cases)

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The following is a preliminary report of seven patients with chronic syphilitic meningo-encephalitis in Springfield State Hospital who had not been helped by the commonly accepted modes of treatment, but who for the most part have shown a favorable symptomatic response to chlorpromazine. This relatively new medication appears to be of benefit even in refractory cases of the disease.

The patients presented below were symptomatically unresponsive to the conventional and accepted methods of treatment, namely: penicillin alone (twelve to fifteen million units, 600,000 units daily for twenty days) or with malaria, 42 hours of fever. None of the patients had improved sufficiently to warrant their return to the community. Two of them presented such severe excitement that their care on the ward was difficult. Some of them were found to be refractory to electroshock, sedation and other forms of custodial management. Some of these patients exhibited persistent delusional systems; others, depressions; and still others, alterations of mood.

The experimental use of chlorpromazine in a patient suffering from an uncontrollable state of delusional excitement produced such unexpectedly successful and dramatic results that other cases were chosen for similar treatment. The patients were selected from the admission, convalescent, and chronic services of Springfield State Hospital. Blood, liver and kidney studies, as recommended by Winkelman and other workers, were made for each patient. Parenteral administration of the drug was used only at the beginning, or until the patient was able to take the oral tablets. Dosages and dose schedules were governed by the amount of medication needed to produce the desired effect. Maximum doses ranged from 150 mgms. to 800 mgms. per day.

Case Studies

Case I: M.A.M., a 39 year old white, male truck driver was admitted July 30, 1954, with a history of positive serology since 1946. He was semi-stuporous and depressed; and required tube-feeding. The blood and spinal fluid showed positive Wasserman reactions. Spinal fluid examinations made August 26, 1954, revealed a total protein of 55 mgms. per cent, 8 cells and a colloidal gold curve of 5543200000. The patient was treated with fifteen million units of penicillin. To relieve him of his state of depression, sixteen electroconvulsive treatments were given between August 3 and September 14. After these treatments, he showed hyperactivity, agitation and elation of such degree that constant sclusion and restraint were required. The patient was beset by vivid delusions and hallucinations, believing that each morning he was brought from another hospital. He failed to recognize any of the nurses and attendants and believed that his ward physician was a lawyer who was trying to get him out of jail.

Chlorpromazine, 50 mgms. TID, was begun September 17, 1954, with immediate response and improvement. The patient came out of the seclusion room; he was free of his hallucinations and delusions, and after a short while began to show good insight into his illness and showed a willingness to cooperate with the hospital staff. Chlorpromazine was reduced to 25 mgms. TID on September 22, and discontinued on October 6, 1954, the date of discharge. On December 27, 1954, the patient returned to the hospital for repeat spinal fluid examination; results were similar except for a slight change in the colloidal gold curve, namely, 5542210000.

Case II: C.C.C., a 45 year old married man, suffering a depressive form of general paresis, had been treated prior to his admission here on May 6, 1953, with fourteen million units of penicillin following a diagnosis of general paresis in February, 1953. On admission the blood Wassermann was positive; the cerebrospinal fluid showed a total protein of 50 mgm. per cent, increased cells, and a paretic

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From Springfield State Hospital, Sykesville, Maryland.

Chlorpromazine used in this study is manufactured by Smith, Kline & French Laboratories, Philadelphia, Pennsylvania, under the trade name Thorazine.

gold curve of 4554321000. The patient was treated with twelve million units of penicillin in May of 1953 without demonstrable change in his spinal fluid. In March, 1954, the patient was given a course of forty-three hours of malaria therapy, following which, in June, 1954, the spinal fluid showed 3 cells, 45 mgms. per cent total protein, and a positive Wassermann and Kahn reaction. The colloidal gold curve was flat. The patient believed himself to be the brother of Jesus and showed extremely poor judgment in his actions. Seven months later the patient's conditions had not changed, and on October 19, 1954, chlorpromazine, 50 mgms. TID, was started, and gradually increased to a maximum dose of 200 mgms. QID. During the final phase of chlorpromazine treatment, electroshock therapy was initiated. In the course of the sixth electroshock treatment, he suffered a fracture of the right femur. The medication seemed to make him all the more depressed and lethargic, without diminishing his delusions and auditory hallucinations. Electroshock therapy and Thorazine were therefore discontinued since neither treatment had been of any demonstrable benefit and the patient remains in the hospital, apparently a chronic custodial case.

Case III: J.K.F., a 37 year old white married man, one of the so-called "expansive general paretics," was admitted March 6, 1954, after an apparently sudden and unexpected onset of the disease, in the course of which he was arrested for refusing to pay a taxi fare while on his way to Washington, D.C., to see the President. He expressed grandiose ideas, asserting, for instance, that he had many thousands of dollars. The spinal fluid findings were confirmatory of central nervous system lues with 9 cells and a colloidal gold curve of 5553210000. The patient was in fair physical condition, restless, agitated and disturbed to such a degree that almost constant seclusion and restraints were required. The patient was treated with twelve million units of penicillin between March 15 and April 4. He was given thirteen electroconvulsive treatments, and, from April 5 to April 13, he received malaria treatments producing a total of forty-two hours of fever. For the most part the patient lay in the seclusion room disoriented and out of contact with his environment, shouting code messages to the stars and uttering strange and inhuman sounds. His treatment appeared to be a complete failure; he seemed doomed to a lifetime of hospitalization on a chronic, disturbed ward. On October 18, 1954, treatment with chlorpromazine was begun, and the dose was rapidly increased to 800 mgms. a day. As the patient was extremely undernourished, he was given double portions of food at each meal. He ate avidly. At first he was spoon-fed, but after a few weeks he was able to feed himself. Soon thereafter the patient was able to come out of the seclusion room; his appetite improved and he gained a total of forty-seven pounds. On December 28, 1954, recheck of his spinal fluid revealed positive Kahn, and a colloidal gold curve of 3221110000. Slowly he began to establish contacts with his fellow-patients and with the ward personnel. He was observed to watch their use of knives and forks at mealtime, and to attempt to re-learn skills he had apparently lost; e.g., one day quite unexpectedly the patient expressed a desire to learn Spanish in order to converse better with his wife, who was of Latin extraction. Encouraged by these results, *push therapy* was begun January 21, 1955. The progressive and satisfactory improvement of the patient led to his parole from the hospital on March 6, 1955. He was described at that time as emotionally flat, but fairly comfortable, and able to make a satisfactory adjustment. The case is to be followed up in our City Out-Patient Clinic.

Case IV: F.M., a 50 year old white married man was admitted for the second time November 26, 1954. He was treated at this hospital August 21, 1953, to September 6, 1953, after a diagnosis of alcoholic hallucinosis and central nervous system syphilis. Spinal fluid examination on August 24, 1953, showed 116 cells and a colloidal gold curve of 5555400000. He was a stooped, confused and disoriented man in poor general condition, with an unsteady gait, slurred speech, a mask-like face and a coarse pill-rolling tremor. He complained of poor memory and vistual hallucinations. During that hospital stay he was treated with twelve million units of penicillin. He reacted to the treatment with improved memory and increased interest in ward activities. He was paroled to his brother and remained out of the hospital until his readmission. At this time the clinical findings were the same as before. These included inability to repeat test phrases, marked hyper-reflexia of all deep tendon reflexes, loss of pain sensation, and a positive Romberg. In addition, there were fine, irregular twitchings of the lips, tongue and hands, and defective coordination in the finger-to-nose test. Serological tests for syphilis were positive. The spinal fluid examination on November 29, 1954, revealed the specimen to be clear, cells 7, total proteins 34 mgms. per cent, Kahn positive, and colloidal gold curve flat, 1100000000. On the ward he was apathetic and depressed. He was treated with penicillin, twelve million units, between December 13 and December 23, 1954, without apparent benefit. Chlorpromazine was started on January 21, 1955, and was soon increased to 200 mgms. QID. He responded quickly, giving evidence of increased interest and socialization, and partially regained memory and insight, to the extent that he was paroled on March 26, 1955.

Case V: P.H., a 44 year old white divorced woman was admitted on March 17, 1954. Prior to this she had received thirty-one electroconvulsive treatments at a private hospital to which she had been admitted because of depression, silly behavior and uncommunicative hostility. Spinal fluid showed a negative reaction for syphilis, but her blood gave positive Wassermann reaction. Her treatment with ECT had brought about some improvement in that she showed less hostility and a more cooperative attitude, however, she remained poorly orientated as

to person and time. Observation at this hospital revealed the patient was confused and irrelevant in her speech and experiencing hallucinations and delusions. The pupils were small and fixed, and did not react to light or accommodation. Blood Wassermann was positive in all dilutions. Spinal fluid examination on March 30, 1954, showed 2 cells, 42 mgms. per cent total protein, positive Wassermann reaction and a colloidal gold curve of 0011000000. When given fifteen million units of penicillin plus ten electroconvulsive treatments, she responded with some improvement in her behavior and attitude; but was still confused and disoriented, and her speech was rambling and illogical. In June of 1954 she was treated with malaria induced fever for 39 hours. Following this she was transferred to the convalescent service, but failed to improve, remaining confused and disoriented as to place. She continued to be withdrawn and refused to take part in ward activities. The nurses described her as irritable and resentful. Her speech remained slurred and her memory impaired. On November 11, 1954, repeat spinal fluid examination revealed no cells, 52 total protein, negative Wassermann reaction and completely flat colloidal gold curve. On February 25, 1955, the patient was started on chlorpromazine which, over a course of several days, was increased to 200 mgms. QID. From the beginning of therapy the patient showed improvement. She became friendly, began to work in the sewing room, and was no longer irritable and negativistic. At the present time she is able to take a more realistic attitude toward leaving the hospital, and an early release is planned.

Case VI: F. M., a 36 year old white married woman was admitted August 30, 1953, in good general condition, but showing confusion, bizarre and irrelevant talk, hallucinations, and delusions. Examination on September 15, 1953, revealed a spinal fluid Wassermann reaction strongly positive, 26 cells, 63 mgms. per cent total proteins, and a colloidal gold curve of 5555321000. The patient received fifteen million units of penicillin. Neurological examination revealed the absence of light reflex, markedly slurred speech, hyperactivity of the deep tendon reflexes and a questionable Romberg. Seclusion was necessary from the beginning of her hospitalization because of her restlessness and agitation. In January and February, 1954, the patient received a course of penicillin and forty-two hours of malaria therapy. This resulted in improvement of the patient's attention and care for herself, but otherwise she continued to have auditory and visual hallucinations, and to be preoccupied with the feeling that her husband was following her. Being extremely fearful of him she refused to leave the ward, cringing there and weeping because she was so upset. Chlorpromazine was begun on February 25, 1955, and subsequently raised to a maximum dose of 200 mgms. QID. There was an immediate change and improvement in her behavior. She now was able to accept a work assignment off her ward and showed a slight euphoria instead of the former depression. She presented in her appearance symptoms of a mild to moderate Parkinson syndrome without tremor, but with mask-like facies, shuffling gait and muscular rigidity. Her comprehension and her interpersonal contacts were much improved. However, there has as yet been no change in her hallucinations and delusions, except that their threatening nature has lessened and she is able to discuss them. It is our intention to continue with treatment, with possibly higher dosages.

Case VII: T.G., a 47 year old white, married woman was admitted March 31, 1954. She had been treated for syphilitic meningo-encephalitis in 1950 with eight million units of penicillin. At that time both the blood and spinal fluid gave positive serologic reactions for syphilis. The latter contained 35 cells and gave a colloidal gold curve of 554442000. Her response to treatment was unsatisfactory. She lacked both insight into her illness and interest in her environment. By the time of her admission to this hospital the patient lost complete moral control of herself; she made a practice of defecating in the sink, as well as being excessively promiscuous sexually. On admission here her blood Wassermann was positive. On April 13, 1954, a spinal fluid examination showed 3 cells, 24 mgms. per cent total proteins, doubtful Wassermann, and a colloidal gold curve of 3332100000. She was treated with fifteen million units of penicillin and then she was subjected to 42 hours of malaria fever between April 28 and May 22, 1954. After this treatment, according to the ward personnel, she was cooperative and pleasant, but without interest in her surroundings. She had occasional grand mal seizures, apparently a manifestation of her meningo-encephalitis. Administration of chlorpromazine was begun on March 12, 1955, maximum dose of 200 mgms. QID, and was soon followed by noticeable improvement in the patient's behavior. She showed an increased interest in her surroundings and in her associations with the other patients. In this patient, too, the blank facies, shuffling gait and stooped posture of Parkinson's syndrome were observed.

Discussion

The successful treatment of clinically unimproved general paretic patients with chlorpromazine opens a new avenue for studies of this disease. Furthermore, it enables us to turn our attention to the chronic custodial wards of our institutions where many deteriorated patients have been given up as far as treatment is concerned.

It is too early to speculate on the rationale of chlorpromazine in the treatment of chronic syphilitic meningo-encephalitis. There is no need to emphasize that it should be considered only as an adjunct to treatment with penicillin, with or without mala-

ria, in those cases still actively psychotic after such treatment.

The best results seem to have been obtained in those patients who have been in an acute agitated state (Cases I and III), and not in those patients whose illnesses were stabilized with systematized delusions (Cases II and VI). The question that remains to be answered is: What are the factors which enhance the action of the drug on the patient's neuropsychiatric symptomatology?"

To search for an answer to this, one has to evaluate the pathology induced by the changes in the brain following invasion by the spirochete. The disease presents many challenging and as yet unanswered problems. General paresis can be defined as a diffuse, parenchymatous inflammatory process caused by the Treponema pallidum, and involving the tissues of the cerebral cortex and the overlying meninges. These diffuse changes show a tendency to occur in the frontal and basal aspects of the brain. It is thus a mental disease, organic in nature, and manifesting clinical, electro-encephalographic, histologic, and chemical changes. These measurable abnormalities of the brain are often reflected in the patient's behavior and patterns of mentation. In the clinical pictures of this disease the whole gamut of neuropsychiatric symptomatology may be seen from depressions and hypochondriasis to manias with increased psychomotor activity, or schizophrenic-like states characterized by hallucinations and delusions. It is up to the worker to evaluate and probe the avenues opened through the research of others in the field of biochemotherapeutics. In general paresis we are concerned with the changes caused by the Treponema pallidum, a diffuse and progressive degeneration of nerve cells which begins primarily in the frontal region, but which, with the extension of the disease, may involve cerebellum, bulb or cortex.

Bateman and Papez,[1] in their timely work on the significance of the thalamus in psychoses, have found that the disease of nerve cells in the thalamic nuclei and cortex in a group of 5 psychotic patients with syphilitic meningo-encephalitis did not differ much from that in patients with other psychoses reported in the same paper. They felt that the hallucinations, delusions and paranoid symptoms were the result of abnormal discharges of thalamus and cortical cells. If chlorpromazine abates those abnormally high discharges in the hypothalamus and thalamus as has been reported by other workers, one could infer that the action of this drug in general paresis is essentially similar to that occurring in other psychoses. The successful treatment in this disease, therefore, would depend on how far the cell destruction of the thalamic nuclei and cortex had progressed in the individual with this disease. One could further speculate that chlorpromazine treatment would give better results in relatively acute cases of general paresis where there is presumably less organic damage (as in Case I and to a lesser extent Case III, in which it is assumed that parenchymatous degeneration is not severe and the emotional disturbances can be ascribed to inflammatory reactions rather than to actual destruction of the neurons). In other words, the patient's prognosis as well as his response to treatment, is dependent upon the reversibility of the inflammatory processes.

The presently accepted modes of treatment of general paresis (penicillin and malaria) aim at arresting the progress of the disease and ridding the brain of the spirochete. In some cases mental symptoms remain after extensive treatment. It appears that chlorpromazine in some of these refractory cases in some manner restores the homeostatic equilibrium of the brain, possibly by altering the irritability of the partially damaged nerve cells and allowing the patient to function on a lower but nevertheless socially acceptable level.

Conclusions

1. Chlorpromazine was used successfully in treating five of seven patients with general paresis who were symptomatically refractory to other forms of treatment (penicillin and malaria). Of the two remaining patients, one showed a fair improvement while the other remained a treatment failure.

2. In none of the seven cases has abnormal liver function been found. Two of the patients

showed Parkinsonism-like states, with characteristic gait and posture. No other complications with chlorpromazine were noted.

3. It seems to have its greatest effect in those cases with strong affective components.

4. In some cases it apparently restores the patient to a socially acceptable level of functioning that will enable him to return to life in the community.

5. It seems to act as an anti-hallucinogen, in some cases abolishing the phantom, in others lessening its threat to the patient.

6. Further study is indicated with a carefully controlled group of patients.

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Premedication for Electroshock Treatment

(Effect of Meprobamate in 120 Psychotic Patients)

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The apprehension and agitation in which the mentally disturbed patient awaits a scheduled electroshock treatment increases the problems of therapeutic management. Fear and resistance to treatment may have been built up in the disordered mind as a result of (a) childhood training to avoid electrical outlets, wiring and appliances; (b) the association of electroshock treatment with the harmful and dangerous effects of electricity in general (pain, burns, shock, electrocution); (c) fear of the mysterious and unknown, and the air of secrecy and isolation surrounding the procedure; (d) fear of unconsciousness, with the possibility of death or loss of control of the faculties; or (e) recollection of previous treatment complications.

Symptomatic relief of pretreatment anxiety is extremely desirable for a number of reasons. A general atmosphere of composure and relaxation in the ward is conducive to successful treatment. In group treatment, the more apprehensive and resistive individuals are likely to be reassured by the behavior of their calmer companions. When preshock tenseness and agitation are alleviated, and the patient is quiet and relaxed at the time the electrodes are applied, the convulsive threshold is lowered, so that less current is required to produce the desired result. With the relief of anxiety, the hazards and complications (electrode burns, tongue bites and other tissue trauma and postshock headache) are significantly reduced. Since post-convulsive excitement and confusion are directly related to pretreatment agitation, less restraint may be required in the postshock period. The course of treatment required may also be shortened.

Urgently needed is a chemical agent possessing active ataraxic and muscle-relaxing properties, that can be administered conveniently to a large group simultaneously, with a minimum of personnel and equipment. The value of the premedication should not be limited by the risk of changes in the blood picture, jaundice, hypotension, tachycardia, laryngospasm or other side-effects.

Many anticonvulsant agents have been studied but none has proved entirely satisfactory for the purpose; none has prevented all or even the commoner complications of electroshock treatment. Most attention has been concentrated on muscle relaxation in efforts to prevent fractures and dislocations, but in general no preparation that successfully obviates such hazards is free of undesirable depressant effects on the respiratory system. In some instances, respiratory arrest has occurred, necessitating artificial respiration.

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Of the series of compounds derived from the 1,3-propanediols,[1] the dicarbamate of 2-methyl-2-*n*-propyl-1, 3-propanediol,[2] or meprobamate, is described as the most potent, possessing marked tranquilizing and relaxant properties, but totally unlike any other tension-lessening agent known. According to published pharmacological and clinical reports,[2-6] meprobamate affects the central nervous system by exerting a selective blocking action on the long interneuronal circuits, especially those between the cortex, thalamus and hypothalamus. The electroencephalographic pattern indicates definite synchronization of the brain waves, with moderate slowing in frequency.[3] Various studies[2-6] have shown that meprobamate relaxes psychic and skeletal muscular tension without depressing the autonomic functions. There is no interference with heart action, respiration, the gastric secretory mechanism or the excretion of sweat, nor is there any effect on the peripheral nerves or myoneural junction. It is stated that the drug is readily absorbed from the gastrointestinal tract and is comparatively nontoxic, hence causes no nausea or vomiting.[2] It is not habit-forming,[4,5] and it does not produce the secondary stimulating action of most sedatives and hypnotics,[5] and induces no tolerance or cumulative effects.[6] It is reported that daily doses as large as 4.8 Gm., continued for six months, produced no adverse reactions. According to one observer,[4] 860 Gm. has been consumed in a fifteen-month period without undesirable results. Overdosage in 2 patients (20 Gm. and 40 Gm., respectively, in twenty-four hours) was counteracted by hot coffee and constant movement for two hours; both recovered.

Method

In this study, meprobamate was used to allay apprehension before electroshock in 120 unselected psychotic female patients, ranging in age from 14 to 65 years. The standard course of treatment was carried out, employing the group technic as commonly used in a large mental hospital. The series was divided into three groups of 40, the patients in each group being treated simultaneously on an open ward, with the beds arranged around the periphery. No screens were set between the beds so that privacy or isolation would not be a factor in any possible calming effect provided by the premedication.

The patients occupying the 20 beds around the right side of the ward received 1 tablet (400 mg.) meprobamate by mouth. Those in the remaining 20 beds, arranged around the left half of the ward, served as controls and received no premedication.

The women, on entering the ward, were allowed to occupy any bed they chose. Those who selected beds on the right side of the room for some treatments chose beds on the left side for others. Thus every patient received pre-electroshock medication throughout about half the course and also acted as her own control.

After a lapse of one hour, electroshock was administered to each patient with the Reiter Electrostimulator, Model CW 47D.

The phases of an electrically produced convulsion generally duplicate the characteristics of a spontaneous seizure. Phase I, the tonic phase (first ten seconds), is usually initiated by rapid flexion of the extremities, probably the result of direct stimulation of the motor cortex, with progressive tonic extension over the course of the ten second period. Phase II, the clonic phase, is brought about by reduction in current at the end of the initial ten-second period. It is characterized by regular rhythmic muscular contractions which continue for thirty to forty seconds, and terminates automatically. In endogenous seizures (epilepsy) this phase occurs spontaneously. Phase III, the respiratory phase, usually follows the convulsive seizure at once, with immediate resumption of respiration, but may be delayed from ten to twenty seconds by a period of apnea. In general, if the clonic phase is prolonged, breathing will begin promptly; conversely, if the clonic phase is brief, a short period of apnea ensues before onset of respiratory activity. Initially, respirations are deep and stertorous, as in comatose patients. In electrically induced convulsions, the respiratory center is stimulated by reduction in current and modulation at the end of the clonic phase, which prevents the cyanosis common to spontaneous seizures.

The entire procedure is completed in forty-five to sixty seconds. The patient generally

awakens in postshock confusion and excitement.

Technic

Group method. The routine method used for more than three years at this hospital, with no mortality and minimal complications, is a modified form of combined convulsive and stimulative electrotherapy utilizing 115 volt, 60 cycle alternating current.

Electroshock is administered in bed rather than on a cart. The beds, with heads against the wall, are spaced 2 to 3 feet apart so that an attendant can stand on either side. The patient lies supine, with a foam rubber pillow under the small of the back to afford hyperextension of the vertebral column, and the head at the foot of the bed. Thus the nurse does not have to reach over the head of the bed to apply the electrodes. The extremities are not restrained in any way.

Application of the electrodes. The scissors type electrodes, as originally supplied with the old electroshock machines, are superier to the handle type dual electrodes or the button type. The scissors type, constructed of aluminum and similar in design to a pair of obstetrical forceps, are equipped with rubber handles and are well insulated. To operate this equipment it is advantageous for the nurse to have long fingers, so that she can manipulate the electrodes readily with one hand.

Each electrode disk is filled with either steel or copper wool (preferably the latter, to avoid rusting), thus forming an egg-shaped surface. This surface is covered with several layers of gauze, which are tied around the disk. To insure good conduction, the electrodes are dipped in saline. A considerable quantity of the solution will be absorbed so that usually the electrodes need to be dipped only once for treatment of the entire ward.

Electrode paste, similar to that used in electrocardiography, is applied to the patient's temples. A mouthpiece of cotton wrapped in gauze and tied at each end so that it resembles a sausage in size and shape, is inserted between the patient's teeth. The chin is grasped by the nurse's left hand, so that the head is held firmly in position. Then, with her right hand, the nurse applies the electrodes to both temples and indicates the patient's readiness for treatment by a brief nod rather than by speaking aloud.

Setting of the instrument. Prior to the start of each treatment, the Reiter Electrostimulator is "Set" in a clockwise direction as follows:

Step 1. The sampler switch is set at sample. With the switch on "Sample," no current flows through the electrodes. It is necessary to keep this switch on "Sample" in order to set the machine. The main switch on the instrument, in the lower left hand corner, is thrown to the "On" position. A red light will then appear in the lower right hand corner and the motor will begin to hum.

Step 2. The switch labeled "Modulation" is then turned to indicate increase—that is, to the right about three quarters of the way, so that the point of the switch is under the tip of the arrow on the label.

Step 3. The switch labeled "Treatment Position" is then turned to position 3.

Step 4. The current intensity switch is turned to indicate increase—that is, to the right until the needle on the ammeter begins to vibrate at 10 ma. The instrument is now set for treatment.

On the nurse's signal of readiness, the treatment is conducted in three phases:

Administration of the electric shock. Phase I. The sampler switch is turned from "Sample" to "Treat" with the left hand. Simultaneously, with the right hand, the current intensity switch is rapidly turned completely to the right so that the needle on the ammeter bounces against the right side of the ammeter at 20 plus, indicating maximum current. The modulation switch is then immediately turned to maximum—completely to the right. This phase is continued for ten seconds, as indicated by the electronic timer in the center of the instrument.

Phase II. The treatment position switch is turned to position No. 1 with the left hand, meanwhile the right hand simultaneously turns the current intensity switch to the left until the ammeter registers 10 ma. The patient will begin to convulse immediately.

Phase III. In about forty seconds, as indicated by the electronic timer, after initiation of treatment, the clonic motions will cease. One of the advantages of this technique is that the convulsion may be suppressed or modified as desired by regulating the current during the clonic phase. Raising the m.a. will diminish the clonus; lowering the m.a. will increase the clonus. Upon cessation of clonus, the current is immediately reduced by turning the current intensity switch, with the right hand, to the left to about 2 to 4 m.a., until the patient's eyes are blinking. Simultaneously, the modulation switch is turned completely to the left with the left hand, so that the needle vibrates slowly at 2 to 4 m.a. This will stimulate the respiratory center so that respirations will begin in ten to twenty seconds. The instrument is turned off and permitted to cool between treatments by turning the sampler switch back to "Sample" and the main switch to "Off." The electrodes are then removed, the patient is turned on her left side, and the pillow is transferred from the small of the back to a position under the head and behind the left shoulder. The electrode paste is immediately wiped off with a wet towel and the skin dried to prevent irritation.

If the start of treatment by the physician can be synchronized with the application of the electrodes by the nurse, the patient usually will offer no resistance to subsequent treatments, because the initial placement of the electrodes will be covered by amnesia. During the treatment the nurse generally perceives a slight tingling sensation in the

hand holding the patient's chin, but this is neither disturbing nor uncomfortable. The attendants standing on either side do not touch the patient during treatment except to prevent rolling from the bed.

Results

Premedicated groups. After receiving meprobamate premedication, all of the patients were quite and noticeably calmer before treatment. All seemed to experience a feeling of well-being. None showed the anxiety and apprehension that are customarily seen in the disturbed patient preceding electroshock treatment. Throughout treatment a general appearance of naturalness and relaxation was displayed by the entire group. (Table 1.)

On the 400 mg. dose the treatment itself was seemingly altered in that the tonic and clonic phases were of slightly less intensity. The most impressive tranquilizing effects were seen in the postshock period, as soon as the patients awakened. The usual immediate postshock confusion was remarkably reduced in a significant number, and in the others was moderately alleviated and shortened. The patients awoke with a clearer sensorium, were able to talk more rationally and coherently, and full consciousness was regained more rapidly than after the control treatments. (Table 1.)

Since headache ordinarily develops, usually within an hour after termination of electroshock, it was remarkable that no premedicated patient asked for aspirin. A number volunteered the information that they were not nervous, felt more relaxed than previously, and that these were the first shock treatments they had ever received from which they did not suffer headache. No postshock restraints were necessary. In no instance was there a fall in blood pressure, which is a frequent sequel to the use of other tranquilizing agents.

Increase of the dose to 600 or 800 mg. did not enhance the clinical response, and at times delayed onset of respiration. As a result, it has been concluded that the optimal dose for premedication of the average candidate for electroshock treatment is 400 mg.

Control treatments: All patients showed some pretreatment tension, strain and apprehension. All were restless in bed, some were agitated and active. All experienced marked postshock confusion (the average length of the confused period was fifteen to thirty minutes.) Eighteen patients (90 per cent) in each of the three groups of control treatments complained of headache and requested aspirin at completion of the procedure.

Previous to premedication with meprobamate, about 90 per cent of patients required aspirin within one hour after return of consciousness. Two tablets, and sometimes more, were usually required by each patient. It was not unusual to dispense a total of 100 aspirin tablets on the days shock treatment was administered.

No side-effects from premedication were observed. No patient experienced vertigo, nausea, vomiting or allergic manifestations.

Comment

For administration of electroshock, the dual handle type electrodes routinely supplied have a number of disadvantages: 1. Both of the nurse's hands are required for application. 2. The surface of the electrode is small, hence burns are frequent. 3. The electrodes tend to slip during the convulsive movements of the patient. 4. The nurse must wear gloves for protection against electric shock or burns if her hands become moist. 5. The electrodes must be dipped in saline prior to each application. 6. Before each treatment, excessive moisture must be wiped off the guards.

The disadvantages of the button type electrodes are: 1. The electrodes must be inserted into a long, flat, thick rubber strap. Accurate placement of this equipment requires delicate and complex manipulation. 2. The band or strap will frequently slip off the forehead. 3. The brass clips which attach to the electrodes often slip off the long metal shank of the electrode or frequently do not make good contact. 4. The metal shank of the electrodes and the brass clip are not insulated or protected, thus may be inadvertently touched by the patient or nurse. 5. To insure adequate contact, the electrodes must be rubbed into the patient's scalp. This frequently irritates the skin. 6. The electrodes must be dipped in saline with each treatment.

Complications of electroshock treatment: 1. Fractures and dislocations (rare in spontaneous convulsions). These injuries are recognized as the commonest undesirable effects. Fractures, most frequently of the vertebral column, are liable to occur at the onset of the tonic phase; are attributable to artificially produced muscular contraction, and are less likely in relaxed, cooperative subjects. Such fractures usually heal rapidly. When the extremities are not forcibly restrained during the course of the procedure, the long bones are not fractured.

2. Respiratory embarrassment may occur (a) as a result of depression of the respiratory center, for which electrical administration of artificial respiration is indicated; or (b) from obstruction of the pharynx by the tongue, for which it is necessary to pry open the mouth and draw out the tongue, thus clearing the airway.

3. Cardiovascular difficulties are exceedingly rare. Chronic endocarditis and myocarditis have been reported, but whether such conditions actually were attributable to the therapeutic procedure is a matter of speculation. Cardiac arrest is even less frequent.

4. Post-treatment perforation of a duodenal ulcer is the commonest of the gastro-

TABLE 1

Controlled Study of Premedication with Meprobamate in 120 Unselected Patients Receiving Electroshock Treatment Administered by the Group Technic, Each Group Consisting of 40 Patients.

	PREMEDICATED GROUPS	CONTROL GROUPS
	400 mg. (1 tablet) meprobamate one hour before electroshock by standard method	*No premedication*
15 min. prior to shock	All lying relaxed, without apprehension, unconcerned with immediate surroundings; but wide awake; no drowsiness. Usually read or looked at magazines. All have soft facial expressions; little conversation, but may talk in soft voices; all respond with smiles to proper stimulus.	All more apprehensive; strained expressions; furrowed brows. Voices high pitched and loud. Most tried to sit up, and twisted sheets in agitation. Some tossed and turned, appearing uncomfortable.
Tonic phase of shock—first 10 seconds	Onset less intense. Forearms drawn toward chest in steadier, more regular action than the usual fast, snapping motion that frequently is responsible for fractures.	Initial response more violent; fast, snapping motion of arms. Some extended entire arm forward, hands bent downward at right angles; others were drawn nearly into upright position, snapping arms toward chest.
Clonic or convulsive phase	Lasted 25 to 30 seconds. Convulsive pattern more rhythmic and less erratic. Color good up to and including period prior to respiratory phase.	Lasted 35 to 45 seconds. Seizure more acute and intense. Noticeably more cyanotic, especially prior to respiratory phase.
Respiratory phase	5 to 6 seconds stimulation.	Average 12 seconds stimulation.
Recovery period	Average 5 minutes. All lying in relaxed positions; soft expressions; all but 1 answered questions rationally. The 1 exception slept for 20 minutes before she responded to questions and had longer period of confusion than others in group.	Average 8 to 10 minutes, some 15 to 20 minutes before response to questions. Confusion lasted two to three times as long as in premedicated groups. All showed tension, some talked loudly, twisted the sheets; about half tried to sit upright.
End of treatment	More alert. Obeyed direction to get up and go for coffee and sandwiches. Walked naturally to pile of slippers at door, selected their own, walked to bathroom, combed hair in normal manner; proceeded down hall in pairs or groups, talking and walking normally.	Longer reaction time. Arose and walked stiffly and hesitantly with strained expressions; had difficulty selecting proper slippers. In bathroom most did not comb hair; merely brushed hands through hair. Walked stiffly to food with strained faces, and very little conversation.

intestinal complications. Hemorrhage from peptic ulcer also has been reported. However, rupture of vessels in the alimentary tract is rare.

5. Although neurologic complications are rare, cerebral vascular occlusions with neurologic syndromes have been reported, as has that of the posterior inferior cerebellar artery syndrome.

Summary

Three groups of 40 (a total series of 120) unselected psychotic female patients in a large hospital for nervous diseases received pretreatment medication with meprobamate to allay apprehension and agitation prior to electroshock. Every patient received 1 tablet (400 mg.) one hour before each treatment throughout about half the prescribed course. Each patient, therefore, served as her own control. In each group, all were treated simultaneously, on an open ward, their beds being placed about two to three feet apart, without screens.

The results were impressive. Under meprobamate premedication, all patients were noticeably calmer and quieter, experienced less postshock confusion, and regained full consciousness more rapidly than the controls. On the 400 mg. dose the treatment itself was only slightly altered in that the tonic and clonic phases were less intense. None suffered the usually inevitable postshock headache, and no after-treatment was required. There was no fall in blood pressure. No side-effects from premedication were observed.

Increase of the dose did not enhance the clinical response. Before the control treatments, all patients showed preshock tension, strain and apprehension; some were agitated and active. All experienced marked postshock confusion, and 90 per cent required aspirin for relief of post-treatment headache.

Author's Note: Meprobmate used in this study is manufactured by Wyeth Laboratories, Philadelphia, Pa., under their trade name, Equanil.

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Observations of Schizophrenic Patients During Psychosurgery Performed Under Local Anesthesia

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Forty-three schizophrenic patients had large frontal craniotomies performed under local anesthesia through which bilateral prefrontal lobotomies were done under direct visualization. Our work was stimulated primarily by the general lack of knowledge as to what happens psychologically and psychophysiologically during and after a prefrontal lobotomy. By performing these operations under local anesthesia we were able to observe the reactions of patients to the following situations: 1) the stress of the long psychological preparation; 2) the stress of the intracranial operation; 3) the electrical stimulation of various portions of the frontal and temporal cortex; 4) the lobotomy proper; 5) the immediate post-lobotomy period. In this paper we would like to present the problems encountered during the

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craniotomies and our observations of what occurs during and immediately following a prefrontal lobotomy.

Of the 43 schizophrenic patients specifically prepared for local anesthesia, only nine had to be given a general anesthetic before the lobotomy itself was done. The remaining 34 patients went through the three to six hour procedures readily managed because of psychological techniques of preoperative preparation and operative management. These techniques will be reported elsewhere.

Observations During Operation

A. Head Preparation

It was unusual for difficulties to occur during this initial phase of the operation. It gave us an opportunity to sample the patients' reactions to relatively mild stress. Usually simple reassurance was enough to manage this phase of the procedure. Where some patients had very low pain thresholds, small amounts of morphine sulphate (0.008 gram) or demerol (0.050 gram) were given intravenously. This gave the necessary analgesic effect plus mild sedation without any interfering somnolence.

B. Work on Scalp and Periosteum

The patient was alerted immediately prior to inserting the needle used to perform the wide field block anesthesia of the scalp. The initial distention of the subgaleal space and stretching of the scalp precipitated marked anxiety in 10 patients who had had considerable difficulties with reality control prior to operation. These reality distortions were grossly magnified by the stretching of the scalp, and we learned that to take prompt action to allay the mounting anxiety for delay in a few instances, necessitated a termination of the local anesthesia. Marked difficulties in patient management during the incision and reflection of the scalp and later of the periosteum was encountered primarily in those patients with whom we had difficulty during the administration of the local anesthesia.

Of the total of nine patients in whom local anesthesia had to be terminated, six occurred during work on the scalp because of rapidly mounting anxiety leading to uncontrollable restlessness. One was a 35-year-old woman who had had a previous topectomy. She, without warning, went into a massive catatonic excitement. Another, a 25-year-old male patient, whose obsessive-compulsive defense mechanisms proved inadequate to contain his increasing tension, became confused and was dominated by frightening auditory hallucinations, so no further contact could be maintained. The other four patients lost reality control and were inaccessible to all of our psychological techniques.

C. Drilling, Sawing and Turning Of Craniotomy Flap

For most patients this portion of the operation was the most trying. The drilling and sawing actually caused no pain of any degree but the magnified sounds and sensations accompanying these procedures caused increased tension in most patients. There was usually a marked increase in restlessness with relatively little verbal expression of the anxiety. One had to be careful not to underestimate the degree of anxiety present even though there were no great affectual or vrbal manifestations.

In spite of the fact that the drilling and sawing caused the greatest degree of anxiety in the largest number of patients only two patients manifested a degree of anxiety requiring termination of local anesthesia. It appeared, in general, that if a patient could go through the long period required for the head preparation and reflection of the scalp, he could go through the psychically more traumatic but much briefer period, required to turn a bone flap.

D. Meninges

The dura, with its rich sensory innervation, is a relatively sensitive tissue. However if it is properly anesthetized, little discomfort is experienced during its incision. The main problem during this phase of the operation was fatigue. The two-to-three-hour period of fatiguing stress plus the residual effects of the pre-operative barbiturates and analgesics, in some of our earlier cases, produced a state of somnolence that was disturbing, since we were about to stimulate the cortex and required an alert patient. Also, there were those patients who required the constant stress of the operation to maintain reality contact. When these pressures were greatly reduced their state of awareness diminished and 12 patients showed in-

creasing restlessness and difficulty with reality control. By keeping the patients alert and aware of the operation we were able to control the anxiety in all of these instances.

Observations During Lobotomy

For descriptive reasons, we divided each frontal lobe into two approximate halves, a medial half and a lateral half, making four quadrants in all that had to be cut. Twenty-nine of 34 schizophrenic patients demonstrated a definite decrease in anxiety during, or just minutes following lobotomy. All 29 presented a definite lessening of the motor component of anxiety, while in 25 the affectual component was ameliorated and in 20 the verbal content was changed.

Just which or how many of the various components of anxiety were affected appeared to depend at least in part upon the amount of frontal lobe white matter cut. It was found that a larger leukotomy was necessary to decrease the affectual aspect than was needed to diminish the motor component. An even greater cut was required to alter the verbal content. The evidence for this rests on the fact that when only two quadrants had been cut 27 patients demonstrated a decrease in muscle tension or other motor activity, while 13 showed a decrease in affect and only one presented any alteration in verbal content. Not until three or all four quarants had been sectioned were changes in verbal content observed. It should be noted that these changes did not appear suddenly but manifested themselves gradually and the improvements increased as the leukotomy was extended.

Six patients had leukotomies performed while they were actively hallucinating. In five the hallucinations either improved or disappeared. It was clearly discernible that the improvements occurred secondary to a marked decrease in anxiety. For example, two patients were hallucinating in all spheres and demonstrated very primitive structuring of their aberrations. When the anxiety was greatly reduced the tactile and olfactory aspects disappeared and the manifest content was better organized. In two others the hallucinations disappeared entirely even before the last quadrant had been cut.

Organic Psychosis Appearing Immediately Following Lobotomy

Nineteen of the 34 lobotomized patients manifested an acute organic mental syndrome, five appearing while the leukotomy was being performed and 14 being noted from one-half to 15 minutes post-leukotomy. It always appeared suddenly manifesting itself by recent memory loss, depression of consciousness, disorientation, confabulations, or an inability to calculate. These organic psychosis varied in intensity. In 12 cases it cleared as suddenly as it had appeared after being present for one-half to 15 minutes. In seven it lasted many hours. In four patients the organic mental syndrome recurred one or more times with intervals of apparent mental lucidity between the psychotic episodes.

Summary

By means of special techniques of preoperative preparation and operative management we were able to take 34 of 43 schizophrenic patients, who could not tolerate the everyday stresses of life, through the several hours required to perform a large craniotomy all under local anesthesia and without great difficulties. In addition to the research advantages of such procedures, these same techniques of management have and can be applied to poor risk neurosurgical and general surgical patients in whom local anesthesia might be considered safer. We have presented some of the more frequent problems that we faced during these operations.

Our studies indicate that the different components of the complexed phenomenon we call anxiety are not equally effected by the same degree of frontal lobe sectioning, that a greater leukotomy was necessary to relieve the affectual aspects than was necessary to ameliorate the motor component and that an even greater section must be made to change the verbal content. We noted that the secondary defense patterns such as obsessions, compulsions, delusions and hallucinations were not improved or permitted to disappear until the anxiety was first measurably relieved. A continued study of the psychophysiological mechanisms behind these observations is proceeding with more specific stereotaxic techniques.

Eastern Psychiatric Research Association

Meeting of December 8, 1955

D. J. IMPASTATO, M.D., *Presiding*

The following discussion represents answers given by the membership to the question, "What has been your experience with reserpine, especially in private practice?"

Dr. Charles Buckman, Kings Park, N. Y.

At Kings Park State Hospital we are currently treating about 1,800 patients with tranquilizing drugs. The ratio is about 2½ to 1 for chlorpromazine over reserpine. Both drugs are given for symptomatic relief of anxiety, tension, excitement and aimless types of aggression. Depressions of any sort will get worse with reserpine. They must be treated with EST. For patients with anxiety associated with psychomotor excitement, chlorpromazine is best. The aggressive type who is pugnacious and has aimless overactivity, does well on reserpine. We begin treatment with 5 mgms. by hypodermic, twice a day, every day for about 7 to 10 days, and then follow with oral medication 3 mgms. daily.

We do not use reserpine in combination with EST.

Dr. Alphonso Telfeian, Albany, N. Y.

About a year ago I treated two patients with reserpine, one was suffering from agitated depression and had bundle branch block. He was treated with reserpine gradually increased to 8 mg. per day (p.o.) and maintained at 6 mg. per day. Patient got over his depression. He was under observation for about 2 months. Another patient was suffering from manic depressive psychosis, depressive type. She did not respond to electric shock treatments. It was decided to try her on reserpine. I could not build up a high dose with this patient. As soon as I would give her more than 6 mg. p.o. per day, the patient would develop bradycardia. At this level reserpine was of no benefit to this patient; but it did not increase the depression.

These encouraging results had to be abandoned as I did not dare to use reserpine after reading the reports of various workers stating repeatedly that reserpine causes depression.

Dr. David J. Impastato, New York City

Reserpine is a symptom antagonizer which I prescribe for symptomatic relief irrespective of diagnosis. In psychoses in private practice where the patients usually are not overactive and cooperative, I have not found reserpine of much help. In depressions it appears useless. In psychoneuroses, especially those showing tension and hostility, it is useful. I have also found reserpine useful in aggression in children, where 1 to 2 drams of the elixir 3 times a day suffices. In a chronic schizophrenic with marked parental aggression, reserpine has helped in holding the patient in remission. Our knowledge regarding dosages and the management of complications in reserpine therapy needs to be augmented. We also know little regarding the possibility of administering reserpine in conjunction with other drugs, especially chlorpromazine, Miltown and Frenquel.

Dr. Remo Cancellieri, New York City

I have found reserpine useful in the very young and the very old. I recall two old patients who had had shock treatment without much benefit. I tried reserpine because they had become disturbed and unmanageable. They responded well and were able to remain at home with relatives on doses from 0.1 to 4.0 mg a day.

Dr. Morton H. Hand, Brooklyn, N. Y.

I have used chlorpromazine chiefly in trying to allay agitation, because of the unpleasant side effects of reserpine. The chief difficulty has been with complaints of pain in the legs, nausea and bowel difficulty. The amount that has been necessary to achieve comparable effects to that of chlorpromazine seems to be somewhere between 4 and 8 mg. of reserpine orally as compared to 300 or 400 mgs. of Thorazine. Because of side effects, I have not been able to continue with it as I would have liked to. The management of the extremely agitated patient who would ordinarily be difficult to control at home, has been one of the indications for giving large intramuscular doses of reserpine. These patients are given an injection of 5 mg. They come back again a few hours later, or remain around the office for several hours, for another. They are subsequently managed by other methods and then are maintained on reserpine orally.

Dr. Theodore R. Robie, East Orange, N. J.

I have had good experiences with reserpine. However, recently I saw a woman with a severe involutional melancholia, who responded to a course of EST. Four weeks later the husband returned and said she was becoming depressed. I put her on reserpine and thought she was progressing satisfactorily during the next few weeks. Then I suddenly received a telephone call and she came to the office, having developed a full blown Parkinsonism on doses of only 1½ mgms. a day. Her mild Parkinsonism cleared up in two days after stopping the drug.

The second patient is currently under my care. She weighs 315 pounds. Before we started treating her, we found on the x-ray marked lipping of almost all the vertebral bodies. We started giving

24 mgs. and later used between 30 and 40 mgs. succinylcholine to modify her EST. She had become severely depressed on the large doses of reserpine she was taking for hypertension. She was taking 1½ mgms. a day of reserpine plus reserpine in combination with apresoline 125 mg tid. She has had 8 EST and is now beginning to develop amnesia. Her blood pressure ten days ago when I started EST was 240. This morning it had gone up to almost 300. I stopped reserpine relatively soon after we started treatment because it was felt that the depression was caused by the drug. Perhaps I was wrong to stop entirely, but the big problem from what I hear tonight is whether reserpine is going to cause depressive reactions of such degree that they will need electroconvulsive therapy.

Dr. Werner Hockstetter, New York City

Reserpine seems to be of considerable help in managing the neuroses but it seems to have less effect in psychoses. Patients that show depressions or have clear-cut depressive trends not only do not respond but should not receive reserpine or chlorpromazine at all. I have seen good responses in cases of "pseudo-neurotic" forms of schizophrenia. These are frequently made more approachable to psychotherapy. I saw the best results in excited schizophrenics and catatonic schizophrenics of short duration.

Dr. Joseph Epstein, New York City

The use of reserpine will perhaps ultimately be restricted to mental hospitals and used for the purpose of quieting disturbed patients. In my personal experience, I have greatly limited its use in office practice. I have found that patients who are depressed are made worse even to the point of becoming suicidal. I have also noted that patients who are on the verge of a depression can be thrown into it by this drug, particularly if there is a history of previous depressive episodes.

Thorazine seems to have a very distinct place in office practice. Its indication is purely for the alleviation of symptoms rather than from the point of view of a diagnostic category. In other words, severe anxieties and fears, irrespective of whether they are associated with severe neuroses, or paranoid states, or other conditions, can in many instances be greatly alleviated if Thorazine is given in sufficient dosage, and for a long enough period.

Dr. K. H. Houck, Flushing, N. Y.

I haven't had too much experience with reserpine. It has been rather disappointing and somewhat unpredictable. When it was tried at the Oceanside Gardens Sanitarium we found that other medications succeeded better in quieting the patients who were likely to be noisy at night or in calming down the manic patients. Of course, when patients were in a marked excitement with confusion and hallucinations, nothing short of E.C.T. seemed to be of any immediate or lasting therapeutic value.

Dr. Frederick L. Patry, Albany, N. Y.

A patient with paranoid schizophrenia of two years duration, with acute symptoms of hallucinations with persecutory trend failed to respond to 12 ECT. I put her on reserpine 2.5 mgsm. 4 times a day. The first night, the patient unknown to her husband, took 2 additional tablets. She started throwing everything around the house, screamed, and was very difficult to control for an hour or so. The next day, she became quite calm, and, for the first time in weeks was able to take care of her three children and household duties. A maintenance dose of .25 mgm 3 or 4 times a day has sufficed. Apparently the initial amount taken was excessive for her and she responded with an aggressive panic reaction which released hostility toward her husband. This effervescent reaction soon subsided and on smaller dosages she is now making commendable 24-hour adjustment.

Dr. William L. Holt, Albany, N. Y.

I'm using less reserpine now than a year ago primarily because of the rather severe Parkinsonism which several of my patients developed, sometimes quite rapidly as in an agitated young man on insulin therapy who suddenly developed marked stiffness and tremor. He was quite depressed about this change.

The other case of Parkinsonism was very late in development. After more than a year on reserpine 2 mgs 4 times a day, this highly neurotic woman developed very marked Parkinsonism. She was getting both Thorazine and Serpasil, which at first seemed to be more effective than either alone. When I stopped the Serpasil the Parkinsonism cleared, some of her tension returned until I gave her Milltown in addition to Thorazine. She came back again and reported a marked improvement in her subjective feelings. Other side effects already mentioned have curbed my use of it in any depression. Recently a recurrent depression of a man of 63 came to me after treatment elsewhere with Serpasil. I changed him to chlorpromazine and sent him home. He called back 2 days later and reported that he was in good spirits.

Dr. D. J. Alamprese, Altoona, Pa.

My experience with the reserpine and chlorpromazine drugs dates back to their early uses. Considering their administration in the neuropsychiatric illnesses, it has been found that proper, adequate, adjusted, individualized dosages have produced good over-all results. The present unreserved medical approval given these drugs, however, is exaggerated, especially the claim that they can supplant electrocerebral therapy in unselected cases.

Dr. Harry Beckett Lang, Albany, N. Y.

I have had more experience with chlorpromazine than with the rauwolfia derivatives. I use reserpine as a drug of second choice in ambulatory office practice but in general hospital practice it might be my first choice. I have found that when depres-

sion is secondary to anxiety then you get good results with chlorpromazine or reserpine. But, if the depression is endogenous, then watch out. I may use dosages of reserpine from .25 mgms. to 1 or 2 mgms. per day, but I check the EKG and the blood pressure very carefully. The situation may be serious if there is a geriatric anxiety depression and the blood pressure drops too fast, because of the resulting acute anxiety to the patient and a possible cardiac or cardio-vascular accident.

Dr. Brian C. Campden-Main, Petersburg, Va.

My experience has been almost entirely limited to the use of reserpine in chronically disturbed psychotic individuals. In our present research, we have been pushing the dosage up to 20 mgs. per day regardless of the appearance of Parkinsonism. It is our impression that Parkinsonism develops, as a rule, on a dosage of from 12 to 16 mgs. per day.

Many of our patients have shown considerable improvement with the drug and it has been our impression that many of them have shown the improvement after they have reached the peak dosage, have shown toxic symptoms, and then have had the dosage reduced.

It is possible that with reserpine we might have to follow a regime similar to that which we use in controlling cardiac failure with digitalis. By this I mean would we have to serpasilize as we would have to digitalize, starting with a high dosage and then reducing the dosage to get optimal therapeutic results?

Dr. Joachim Luwisch, New York City

I have had several patients who received electro-convulsive treatment, together with Serpasil. Among those patients were patients whom I had treated before wiht electro-convulsive therapy. Some of them had come back the third or fourth time. The patients suffered from involutional or agitated depressions. While on previous occasions the number of treatments needed were between eight and ten, this time the number of treatments exceeded the usual number by at least fifty to sixty percent. My feeling is that the medication of Serpasil delayed the recovery under electro-convulsive therapy.

Dr. N. S. Kline, Orangeburg, N. Y.

I will try to answer some of the questions raised. Dosage of reserpine is extremely important. There is no set routine for all circumstances. In an emergency one should not treat a disturbed, assaultive psychotic individual with 25 mg. of chlorpromazine or even 3 mgms. of oral reserpine. This is a waste of the drug. If you are going to use pharmacological treatment, really use it. With chlorpromazine in acute cases of this type we start with 600 to 900 mgms of chlorpromazine a day. With reserpine we usually start with 5 to 10 mgms. intramuscularly and 3 mgms orally.

In the mildly psychotic seen in office practice or in the neurotic the dosages are less and the results are not immediately noticeable. Noticeable effect, usually requires a number of weeks. The trial of the drug is not adequate unless the patient is kept on it for at least two or three months. The patients should be cautioned not to expect immediate improvement although this sometimes does occur. It is our impression that reserpine will act to set aside the usual ego defenses which the neurotic or psychotic sets up against underlying drives. As a consequence much new material rises up to the surface. Increased enjoyment of physical activity, of food and increased erotic desires are frequent but also underlying anxiety or depression also may appear. I have had a number of such cases probably best typified by one patient who was in an acute anxiety state of long duration. She spent her energies "holding on to herself." She was so tense that she could not sit down during the entire interview. I gave her 10 mgms of reserpine intramuscularly. She went home and had quite a time. The elevator operator in her building had been browbeating her for years and she dared not reply for fear that her hostility would get out of hand. This day she really put him in his place. On entering her apartment she found her 9 year old child still awake (it was 11 P.M.). She swatted the child on the rear-end, something she had never done before, with therapeutic results. She had a real brawl with her husband and fired the maid who was incompetent but frightening. Whereas reserpine seems to set aside the defenses, chlorpromazine seems to strengthen them. The choice of one or the other drug (or the combination) may be determined by psychodynamic considerations.

In a recent paper (Kline, Barsa and Gosline) we reported on the side effects of such treatment. I would like, however, to emphasize that there does appear to be lowered resistance to intercurrent diseases. In patients in whom depression or anhedonia develops, we have found a few ECT's at the termination of treatment to be helpful in curing the patient of the "cure." Cogentin and Doriden were useful in controlling other side effects. Boudwin and I have found that some patients treated as long as six months who had not responded adequately during treatment, did improve after the drug was discontinued. The dose of reserpine which we use in private practice varies from 0.1 mgms a day to as high as 10 mgms. Although the new pharmaceuticals have certainly not emptied the hospitals they have brought about the discharge of certain patients who otherwise would not have been released and I can say without hesitancy that there is not a single hospital psychiatrist who would want to go back to the days before these medications were available. The improved comfort and safety of the patients and their accessibility and amenability is a revelation.

Editor's Note: Chlorpromazine is manufactured by Smith, Kline & French laboratories under the trade name Thorazine. Reserpine is manufactured by Ciba Pharmaceuticals under the trade name Serpasil.

Book Reviews

PRACTICAL NEUROLOGY by Leo M. Davidoff, M.D., Prof. and Chairman, Dept. of Surgery of the Albert Einstein College of Medicine, and Emanuel H. Feiring, M.D., Associate Prof. of Surgery (Neurosurgery), Albert Einstein College of Medicine. Cloth. $7.00. Pp. 442. McGraw-Hill Book Co., Inc., 330 West 42nd Street, Nw York, N. Y., 1955.

As the authors suggest, the book is not an encyclopedic reference on the subject of neurology. However, in reviewing the book I find a well organized descriptive approach which should serve in a practical manner for the student, resident, as well as the practitioner who may desire a clinical refresher on the neurological aspects of an examination.

The book is up to date in respect of the subject contents, and in methodical style skillfully covers in respective chapters, the neurological involvement and specic identification of the varying clinical syndromes with suggested medical and/or surgical treatment of vascular lesions of nervous system traumata, of neoplastic and inflammatory diseases, of diseases of unknown etiology, of congenital and heredodegenerative diseases, of diseases due to toxins, and concludes with a well organized chapter on the metabolic diseases in so far as they are clinically associated with neurologic manifestations. The book is well indexed and should prove of practical value to those interested in the subject.

Lewis J. Siegal, M.D., LL.B.

PRESENT DAY PSYCHOLOGY. Edited by A. A. Roback. Philosophical Library, New York. Pp. 995. $12.00.

This survey is certainly one of the most comprehensive reviews of present day psychology thus far encountered. A compilation of forty original contributions, three of them written by the editor, the scope of the work affords us a broad and fair view of all psychological trends and topics. Recognizing that "no man can possibly master more than a segment of his science," the author overcomes his doubts about the value of anthologies such as this and presents the work of men who are authorities in hetir particular branch of the psychologic discipline. All things considered, this is a prodigious work and undoubtedly the task was worthwhile. It will almost certainly be a ready reference for a long time to come.

Strangely enough, the unevenness usually expected in a compilation such as this, the work of many hands, is not particularly apparent. This in itself is testimony to the skill of all concerned. Here in one volume are to be found essays upon subjects so seemingly disparate as the Experimental Parapsychology of Rhine, to the Psychology of Religion by Vergilius Ferm, and from the Recent Findings in General Neurology by Keegan, to the Psychology of Literature by the editor. The thread of Ariadne, which binds these chapters together, is the broad knowledge of the editor.

Obviously it is impossible to adequately review a work such as this without writing a companion volume equal in size to the one under scrutiny. Some of the essays will appeal to the psychiatrist and physician; some will not. Yet all are written fairly comprehensively and evidently in accordance with editorial directives. For anyone who is desirous of an overall view of the present status of psychology, including the clinical and the dynamic, this book will be highly desirable. The volume will have to be sampled; the offering is too vast for continuous reading. It is an excellent reference volume and as such it is recommended.

Francis J. Braceland, M.D.

BOOKS RECEIVED

LEWIS J. SIEGAL, M.D., LL.B.

PSYCHOANALYSIS — PRACTICAL AND RESEARCH ASPECTS by Willi Hoffer, M.D., Ph.D., Editor. The international Journal of Psycho-Analysis. Cloth. $3.50. Pp. 102. Williams and Wilkins Company, Mount Royal and Guilford Avenues, Baltimore 2, Maryland, 1955.

NEURO-VASCULAR HILA OF LIMB MUSCLES by James Couper Brash, M.C., M.A., D.Sc., LL.D., F.R.C.S. Ed., F.R.S.E., Professor Emeritus of Anatomy, University of Edinburg. Cloth. $7.00. Pp. 100 with illustrations. The Williams and Wilkins Company, Mount Royal and Guilford Avenues, Baltimore 2, Maryland, 1955.

EPILEPSY AND THE FUNCTIONAL ANATOMY OF THE HUMAN BRAIN by Wilder Penfield, O.M., C.M.G., M.D., and Herbert Jasper, M.D., C.M., B.A., and Chapter 14 by Francis McNaughton, B.A., M.D. Cloth. $16.00. Pp. 896 with 8 color plates and 314 black and white illustrations. Little, Brown and Company, Boston, Mass., 1954.

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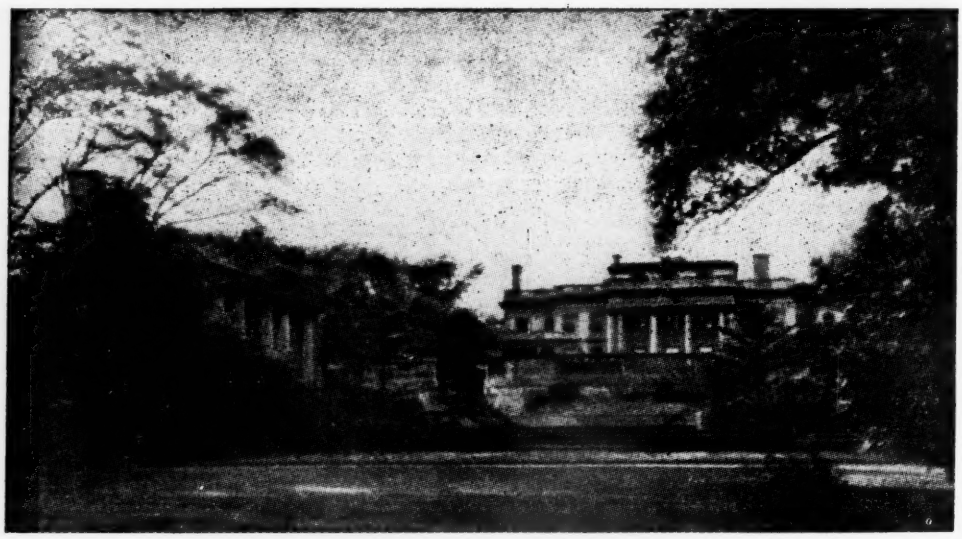

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